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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/079,834	05/15/98	MOUNTZ J	D6005

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EXAMINER	
TUNG, M	
ART UNIT	**PAPER NUMBER**
1644	10

DATE MAILED: 10/29/99

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/079,834	M untz And Zhou
Examiner	**Group Art Unit**
Mary B. Tung	1644

☒ Responsive to communication(s) filed on *Aug 27, 1999*

☒ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *1, 3-6, 8, 9, 16, and 17* is/are pending in the applicat

Of the above, claim(s) _____ is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1, 3-6, 16, and 17* is/are rejected.

☒ Claim(s) *8 and 9* is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

— SEE OFFICE ACTION ON THE FOLLOWING PAGES —

Serial No. 09/079,834
Art Unit 1644

DETAILED ACTION

Election/Restriction

In light of the paper filed 8/27/99, Paper No. 9, only the following rejections remain:

Claim Rejections - 35 U.S.C. § 102

1. Applicant's arguments filed in Paper No. 9 have been fully considered but they are not persuasive.

2. Claim 17 stands rejected under 35 U.S.C. 102(e) as being anticipated by Bellgrau (US Patent #5,759,536), for the same reasons set forth in the actions mailed 10/27/98, Paper No. 4 and 4/21/99, Paper No. 7.

3. The Applicants argue that in Bellgrau's method, the donor organ tissue and the Fas ligand are introduced to the recipients through different routes and at different times and that claim 17 has been amended to recite specific order in which the donor organ tissue and the Fas ligand are to be administered, i.e., the donor organ tissue is perfused with Fas ligand first and then the perfused donor organ tissue is introduced to the recipient. The amendment does not overcome the rejection and the argument is not persuasive because the recited method would be encompassed by the cited teaching because the islets of the '536 patent are perfused donor organ tissue. The claims have no recitation that would preclude the continuing perfusion of Fas ligand after transplantation and therefore, interpreting the claim broadly, would be encompassed by the '536 patent. Also, in response to Applicants arguments that the present invention uses donor tissue that has been engineered to not express Fas ligand, this limitation is also not recited in the claim. Therefore, the reference teaching anticipates the claimed invention and the rejection is maintained.

Claim Rejections - 35 U.S.C. § 103

4. Claims 1, 3-6 and 17 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Bellgrau (US Patent No. 5,759,536) in view of Süss (Z), for the same reasons set forth in the actions mailed 10/27/98, Paper No. 4 and 4/21/99, Paper No. 7.

5. The Applicants argue that Bellgrau does not teach nor suggest antigen presenting cells which express Fas ligand and an antigen or the use of such antigen presenting cells for inducing systemic tolerance to the antigen. The Applicants repeated their arguments concerning the '536 patent, discussed, *supra*. The Applicants additionally teach that Süss does not teach or suggest a method by using antigen presenting cells expressing Fas ligand and the antigen to induce systemic tolerance or teach a method of decreasing

rejection of a graft by administering Fas ligand perfused donor organ to an in-need individual. In response to Applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Additionally, the differences alleged by Applicants between the reference teachings and the claimed invention are features which are not claimed. One of ordinary skill in the art at the time the invention was made would have been motivated to use Fas-ligand-expressing dendritic cells, taught by Süss in the method of antigen-specific immunosuppression in order to improve transplantation success or for the treatment of an autoimmune disease such as diabetes, as taught by the '536 patent (see the abstract and col. 3, lines 51-55, in particular). From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole is *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

6. Claims 1, 3-6 and 17 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Bellgrau (US Patent No. 5,759,536) in view of Schuler (Y), for the same reasons set forth in the actions mailed 10/27/98, Paper No. 4 and 4/21/99, Paper No. 7.

7. The Applicants argue that Schuler (Y) is a review article which does not demonstrate a method of inducing antigen-specific systemic tolerance by administering antigen presenting cells expressing Fas ligand and the antigen. The Applicants repeated their arguments concerning the '536 patent, discussed, *supra*. In response to Applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). However, Schuler teaches that dendritic cells express Fas ligand and may provide a novel approach to induce tolerance in transplantation and autoimmunity (see the abstract, page 320, col. 2, paragraph 2, and page 321, col. 2, in particular). Dendritic cells are well known in the art to be antigen presenting cells. Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to use Fas-ligand-expressing dendritic cells, taught by Schuler in the method of immunosuppression taught by the '536 patent in order to induce tolerance for the treatment of transplantation or autoimmune disease such as diabetes, as taught by Schuler. From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole is *prima facie* obvious to one of ordinary skill in

the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

8. Claim 16 stands rejected under 35 U.S.C. 103(a) as being unpatentable over Bellgrau (US Patent No. 5,759,536) in view of Süss (Z), for the same reasons set forth in the actions mailed 10/27/98, Paper No. 4 and 4/21/99, Paper No. 7.

9. The Applicants argue that "Bellgrau, et al. do not teach the use of antigen presenting cells which express Fas ligand and an antigen specific to the graft in their method." The Applicants additionally argue that "Süss, et al. does not teach or suggest a method of creating immune-privileged sites in an in-need individual to decrease the rejection of a graft using Fas-ligand-expressing antigen presenting cells, or specifically dendritic cells. In fact, Süss et al. cites prior art for the killing of T cells to create immune privileged sites by the expression of Fas ligand by Sertoli cells or parenchymal cells". In response to Applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Additionally, the claims merely recite the induction of systemic tolerance, which would be encompassed by the teachings of Süss on page 1795. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to use Fas-ligand-expressing dendritic cells, taught by Süss in the method of immunosuppression taught by the '536 patent in order to improve transplantation success or for the treatment of an autoimmune disease such as diabetes, as taught by the '536 patent (see the abstract and col. 3, lines 51-55, in particular). From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole is *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

10. Claim 16 stands rejected under 35 U.S.C. 103(a) as being unpatentable over Bellgrau (US Patent No. 5,759,536) in view of Schuler (Y), for the same reasons set forth in the actions mailed 10/27/98, Paper No. 4 and 4/21/99, Paper No. 7.

11. The Applicants argue that Schuler et al. "provides no data or even suggestion of a method of creating immune-privileged sites in an in-need individual to decrease the rejection of a graft using fas-ligand-expressing antigen presenting cells, or specifically dendritic cells. In response to Applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually

where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). However, Schuler teaches that dendritic cells express Fas ligand and may provide a novel approach to induce tolerance in transplantation and autoimmunity (see the abstract, page 320, col. 2, paragraph 2, and page 321, col. 2, in particular), providing the necessary statement of motivation or suggestion to combine the references. Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to use Fas-ligand-expressing dendritic cells, taught by Schuler in the method of immunosuppression taught by the '536 patent in order to induce tolerance for the treatment of transplantation or autoimmune disease such as diabetes, as taught by Schuler. From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole is *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

12. The Examiner maintains that the article by Chen and Wilson, provided by the Applicants with Paper Nos. 5 and 6, is not pursuasive, because even though the authors discussed the "ingenuity" of the invention, does not provide evidence that the cited teachings of Süss (Z) and Schuler (Y) do not encompass the claimed invention. The Applicants argue the article by Chen post-dates both the Süss and Schuler references and reason that "if the teachings of Süss and Schuler rendered the present inventions obvious, the inventions would not have been considered "ingenious" by Chen and Wilson." However, the reference by Chen and Wilson do not clearly point out the *patentable* novelty which the Applicants think the claims present in view of the state of the art disclosed by the references cited or the objections made. Further, they do not show how the amendments avoid such references or objections. They are opinions not based in the legal definition of 35 U.S.C. 103(a).

Allowable Subject Matter

13. Claims 8 and 9 stand objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

14. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. 1.136(a).

15. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R. 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

16. Papers related to this application may be submitted to Group 1640 by facsimile transmission. Papers should be faxed to Group 1640 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). THE CM1 FAX CENTER TELEPHONE NUMBER IS (703) 305-3014 or (703) 308-4242.

17. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Mary Tung whose telephone number is (703)308-9344. The Examiner can normally be reached Tuesday through Friday from 8:30 am to 6 pm, and on alternating Mondays. A message may be left on the Examiner's voice mail service. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1640 receptionist whose telephone number is (703) 308-0196.

Mary B Tung

October 28, 1999
Mary B. Tung, Ph.D.
Patent Examiner
Group 1640

David A. Saunders

DAVID SAUNDERS
PRIMARY EXAMINER
ART UNIT 182 / 644